R E M A R K S

Support for new claim 19 is in claim 16 and in the specification at page 2, lines 17-19.

The rejection based on the first paragraph of 35 U.S.C. § 112 is respectfully traversed. As to the specification, this is stated "as failing to provide an enabling disclosure and an adequate written description of the invention."

That applicants disclose their method as an alternative to liposuction is true. Also, it is not contested that with liposuction, adipose tissue "is physically removed from the body, thereby reducing the absolute amount of fat present in the body at selected sites compared to those sites prior to the treatment" (Office Action, page 3, lines 8 - 11).

But it is also true that applicants' invention, as claimed and as disclosed, reduces "the absolute amount of fat present in the body at selected sites compared to those sites prior to treatment":

> "a dissociation and reduction of the adipose tissue at that location occurs. In a single treatment, reduction of the tissue from its original volume may range from 25% to 75% and higher" (specification, page 2, lines 15 - 19).

This provides several advantages over liposuction (specification page 2, line 19 through page 3,

line 9), e.g. it avoids incisions, risk of infections, mechanical trauma, risks of contour deformities and mechanical injuries to adjacent tissues and anatomical structures.

The Examiner is concerned with the fate of fat liberated by applicants' procedure, pointing out that in liposuction it is physically removed from the body. At page 6, lines 24-25 of the specification applicants teach that "Residue from the adipose tissue in the treated location is at least party metabolized", but this is dismissed as "in no way shown this to be true in a degree significant for the intent of the claimed invention" (Office Action, page 3, lines 17-18). Such a showing is not properly required. The mechanisms of fat metabolism are well understood by those skilled in the art. For instance, the following from "Introduction to Fat Metabolism," a course by Dr. David Adams, School of Pharmacy & Medical Sciences, University of South Australia, Adelaide,

http://www.prm.unisa.edu.au/h&p2fat.htm

> "When required, the stored triglycerides are released from the adipose tissue, a process catalyzed by mobilizing lipase which is stimulated by adrenaline and glucagon, the same hormones which stimulate release of stored glycogen as glucose.

> "When released from the adipose tissue, the fatty acids are transported attached to the major protein in the circulation, which is albumin. Fatty acids are transported to various tissues by this means and then oxidised."

The Examiner herself acknowledge that the fat released by applicants is ultimately metabolized: "... the fat present in the body will be maintained at its present level and will be deposited in adipocytes, either remaining at the site or at other sites, until metabolized" (Office Action, page 7, lines 20-23). Since the released fat is, in the end, metabolized by oxidation, it would appear that the Office Action is concerned with the rate of the metabolism, not whether it in fact occurs. As to where the fat goes, it is known that the oxidation occurs at two locations in the body, i.e. in muscles and in the liver (Adams, op. cit., supra).

The Office action calls for metabolizing "in a degree significant for the intent of the claimed invention". But what is the intent? Nowhere will it be found that applicants' express an intent other than that the amount of adipose tissue at selected locations in the body be reduced. That liposuction immediately reduces does not affect applicants' intent for localized reduction, or require that the latter occur at any particular rate. That "In a single

treatment, reduction of the tissue from its original volume may range from 25% to 75% and higher" clearly meets the intent of "reduction of the adipose tissue at that location", no matter what ultimately happens to the fat, and when.

If a liposuction patient should demand reduction of overall body weight, in addition to reduction in amount of adipose tissue at the selected location, the physician might advise him or her that liposuction "has been used as a staged procedure for weight loss with questionable success" (Applicants' specification, page 1, lines 11-12).

The Office Action states that "the fat is still present in the body and the body must deal with it in some manner." The foregoing shows that the manner, by the Examiner's own admission, is metabolizing, i.e. oxidation as is known by the art.

The Office Action points to the fact that rats treated for 14 days gained weight (note that the rats were fed ad libitum, specification, page 24, lines 7-8), and then contends that it must matter where the fat goes if nothing is removed from the body, and that, as fat has weight, an increase in weight must matter. Applicants' intent has nothing to do with whether released fat remains in the body

or is metabolized, or whether the patient as a result of the treatment loses or gains weight.

It is respectfully submitted that it is improper for the Office to impute weight loss as a necessary attribute of applicants' invention. It is not a necessary attribute of liposuction, except to the extent that the fat removed will instantaneously reduce the weight by just that amount (which will be a small percentage of the patient's total weight). If the daily ingestion of fat continues, and if the patient eats ad libitum, as did applicants' rats, then he/she can expect weight increases.

The Office Action relies on Guidicelli et al. to show that rat adipocytes react in a metabolically different manner from human adipocytes particularly when treated with collagenase and trypsin. While this was true with respect to certain added biological entities, the reference discloses that a mixture of collagenase and trypsin "failed to affect the spontaneous rate of glycerol and free fatty acid release from both fat cell species" (rat and human). (As pointed out above, released fatty acids are transported in the circulation to the tissues wherein they are oxidized). The same rate of release from both rat and human fat cells indicate that the rat is not an unreasonable

model. Reduction of the amount of adipose tissue at the site of treatment in rats leads to the reasonable expectation that the same will occur in humans. Applicants have provided an adequate written description and an enabling disclosure.

Rejection of the claims under 35 U.S.C. § 112, first paragraph is believed overcome for the reasons discussed above.

Rejection of the claims under 35 U.S.C. § 103 as being unpatentable over Lee et al. combined with Guidicelli et al. is respectfully traversed.

The Office relies on Lee et al. (supplemented by Guidicelli et al. for collagenase plus trypsin) for the holding that it would have been obvious and predictable to use conventional enzymes known to digest adipose tissue regardless of the site of the expected digestion, i.e. dissociating the cells of the tissue at any location in the body or in tissues outside of the body.

It may be noted that the Examiner is of the opinion, in holding lack of enablement, that the practitioner would be required "to engage in an undue amount of experimentation to practice the claimed invention and the practitioner would still not have a reasonable expectation of success" (Office

Action, page 4, last paragraph). These are classic criteria for non-obviousness.

Ever since far back in recorded history, and perhaps beyond, many humans have developed fat where they did not want it. When it was found that such fat could be suctioned out, liposuction was born. In recent decades use of the procedure has grown greatly, despite its several drawbacks (applicants' specification, page 2, lines 3-8). Parallel to this development, Rodbell in 1964 used collagenase to isolate fat cells, Fain, et al. in 1969 added trypsin during the digestion of adipose tissue by collagenase [both cited by Guidicelli et al.], Guidicelli et al. followed suit in 1976. All these were in vitro. Also paralleling the growth of liposuction, collagenase was being used in vivo for therapeutic treatment of a variety of human clinical conditions (Lee et al., column 1). Yet in all these years, no one thought to use collagenase, rather than liposuction, to reduce the amount of unwanted adipose tissue at specific locations in the body.

Lee et al. disclosed using purified collagenase plus purified chymopapain for digesting connective tissues, and included several working examples of treating adipose tissue in vitro to isolate microvessel cells embedded therein.

When it comes in vivo, Lee et al. specify eight different bodily conditions that can be treated with their enzyme compositions (column 8, lines 1-7). Yet subcutaneous fat, or fat of any kind, is not mentioned. Thus Lee et al. are perhaps the most recent among the workers in the field who have not come up with applicants' invention.

It is submitted that this long history cannot be ignored to reach the conclusion of obviousness and predictability. Lee et al. actually chose liposuctioned fatty tissue to treat in vitro with their collagenase plus chymopapain but remained oblivious to a connection with their long list of human conditions they treat in vivo.

Reconsideration and allowance of the claims is courteously solicited.

Respectfully submitted,

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